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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,122	12/23/2005	Makoto Ono	282359US0PCT	5544

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EXAMINER
LOEWE, SUN JAE Y

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
05/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/562,122	ONO ET AL.	
	Examiner	Art Unit	
	SUN JAE Y. LOEWE	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *5 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☒ Claim(s) *1-4, 6, 7 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12-23-2005; 3-29-2006; 8-18-2006; 9-5-2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-15 are pending in the instant application.

Election/Restrictions

2. Applicant's election without traverse of Group I, and Type-II crystal of compound (I) as a single species, in the reply filed on March 3, 2008 is acknowledged. The elected species is the polymorph of sodium trans-4-[1-[2,5-dichloro-4-[(1-methyl-1H-3-indolylcarbonyl)amino]phenylacetyl]-(4S)-methoxy-(2S)-pyrrolidinylmethoxy]cyclohexanecarboxylate pentahydrate identified by the *full* XRD pattern of Figure 4 - top (instant specification pg. 5).

3. MPEP § 803.02 provides the following guidelines:

"Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable **, the provisional election will be given effect and examination will be lim-

ited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration."

The Markush-type claim(s) encompassing Applicant's elected species was not allowable (see Sections 7 and 8). Thus, the provisional election was given effect and the non-elected species were withdrawn from further consideration.

4. Claims 5 and 11-15 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on November 8, 2007.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statements (dated December 23, 2005; March 29, 2006; August 18, 2006; September 5, 2006) were in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The statements were considered. Signed copies of form 1449 enclosed herewith.

Claim Objections

7. Claims 1-4 and 6-10 objected to for containing non-elected subject matter. Elected subject matter: Type-II crystal identified by the *full* XRD pattern shown.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 8 and 9 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
The claims are drawn pharmaceutical compositions, comprising the instantly elected species, for intended use of preventing or treating "disorder caused by cell adhesion."

"Disorder caused by cell adhesion" broadly encompasses oncologic (cancer), immunologic (eg. HIV) and inflammatory disorders. See claim 9.

The nature of the invention
Support for the intended use is based on the in vitro inhibition VLA-4 by the instantly elected species (specification pg. 17).

The state of the prior art/level of ordinary skill/level of predictability
The inhibition of VLA-4 has been primarily investigated in the area of treatment of multiple sclerosis (MS), which is a lifelong chronic disease that cannot be prevented or cured (Multiple Sclerosis, pg. 1of 19).

Following is the state of the art for the treatment of MS with VLA-4:

- VLA-4 develpment halted in 2005 due to safety concerns, which creates obstacles for *emerging* therapies such as MS (www.redorbit.com)
- ATL1102 – the results for clinical trials Phase IIa for treatment of MS not predictable; the results are contigent on completion of research and development (www.marketwire.com)
- CDP323 – entering clinical trials Phase II – expectation that they may not be able to demonstrate the safety and efficacy is stated (www.medicalnewstoday.com)
- Conclusion:
  - Prevention of MS is not possible in the current state of the art
  - VLA-4 inhibition as an etiology for the treatment of MS is "nascent technology"
  - VLA-4 inhibition as an etiology for the treatment of MS appears to be unpredictable

The art of utilizing VLA-4 inhibitors for the treatment of diseases other than MS is also nascent and unpredictable. Moreover, evidence suggests a high level of unpredictability. See representative facts for below (www-redorbit-com):

- The future of VLA-4 antagonists for treatment in therapeutic areas other than MS is less certain
- Natalizumab, a VLA-4 antagonist, was in development for treatment of Crohn's disease however safety concerns limited its indication
- Other VLA-4 antagonists for Crohns disease have been discontinued owing primarily to limited efficacy

The amount of direction provided by the inventor/existence of working examples
No working examples are provided in the instant specification. The guidance/direction is limited to the in vitro inhibition of VLA-4 by the instantly elected species.

The quantity of experimentation needed to make or use the invention
In the absence of working examples/direction, enablement rests on the existence of an art recognized predictable correlation between the disclosed activity and the claimed use.

Evidence suggests that this requirement is not met for the instant case because, for the reasons discussed above, antagonism of VLA-4 does not reasonably correlate with the treatment of the scope of "disorder caused by cell adhesion."

MPEP 2164.01(a) states:

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
>
> (A) The breadth of the claims;
>
> (B) The nature of the invention;
>
> (C) The state of the prior art;
>
> (D) The level of one of ordinary skill;
>
> (E) The level of predictability in the art;
>
> (F) The amount of direction provided by the inventor;
>
> (G) The existence of working examples; and
>
> (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the evidence regarding each of the above factors (see discussion above), the specification, at the time the application was filed, would not have taught one of ordinary skill in the art how to practice the full scope of the claimed invention without undue experimentation.

Based on the above analysis, the scope of the instant claims lack enablement.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe, Ph.D./
4-21-2008

/Kamal Saeed, Ph.D./
Primary Examiner
Art Unit 1626